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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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IMMUNEX CORPORATION
LAW DEPARTMENT
1201 AMGEN COURT WEST
SEATTLE, WA 98119

EXAMINER	
RAO, MANJUNATH N	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 02/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/024,828	VIRCA ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,11-20 and 24-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,11-20 and 24-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-7, 11-20, 24-29 are currently pending in this application. Claims 1-22 are currently pending and are present for examination.

Applicants' amendments and arguments filed on 11-24-03, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. Examiner has withdrawn the rejection under 35 U.S.C. 112, 2nd paragraph in view of the claim amendments.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4, 17, 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 4, 17, 28 recite the phrase "recombinant polypeptide is a purified polypeptide". It is not clear to the Examiner as to whether applicants are referring to a "purified recombinant polypeptide" or to a non-recombinant "purified polypeptide", i.e., purified from its natural source. A perusal of the specification did not provide a clear definition and therefore, Examiner requests a clarification. However, for examination purposes Examiner has broadly interpreted the phrase to include both purified recombinant and purified non-recombinant (i.e., purified from its natural source) polypeptide.

Claims 5, 18, 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 5, 18, 29 recite the phrase "produced by cells". It is not clear to the Examiner as to whether applicants are referring to a "recombinant cell" or to a non-recombinant cell. A perusal of the specification did not provide a clear definition and therefore, Examiner requests a clarification.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7, 11-20, 24-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of screening a candidate molecule as an antagonist or an agonist of a polypeptide by determining the ability of the compound to modulate the phosphorylation --of its specific substrate-- activity of the polypeptide, does not reasonably provide enablement for any such method wherein any substrate is used in such a phosphorylation assay or wherein the substrate for the phosphorylation activity of the kinase is unknown or not provided. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3)

the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-7, 11-20, 24-29 are so broad as to encompass a method of identifying candidate compounds which modulate the phosphorylation activity of the polypeptide using any substrate. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of substrates broadly encompassed or when no substrate is encompassed at all. Since it is well known in the art that kinases have specific substrates and not all substrates can be phosphorylated by all or any kinase/s, using any or all substrates for such a method as above, requires a knowledge of and guidance with regard to the way the assay needs to be performed. Therefore use of the polypeptide for identification of compounds that modulate its phosphorylation activity requires a knowledge of and guidance with regard to the substrates that can be used in setting up and interpretation of results of such assays. However, in this case the disclosure is silent regarding specific substrates that can be used in such assays. In view of the lack of guidance it would require undue experimentation by the skilled artisan to make and use the claimed method. The specification is limited to teaching that the polypeptide is a kinase but provides no guidance with regard to methods of identification of compounds that can modulate its activity. In view of the great breadth of the claim, amount of experimentation required to identify the substrates, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), the claimed invention

would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

The specification does not support the broad scope of the claims because the specification does not establish: (A) a rational and predictable scheme for identifying compounds which modulate the phosphorylation activity of the polypeptide using s specific substrate/s and (B); the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of compounds having the desired characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous Office action, applicant argues that claims have been amended to replace the previously used phrase "biological activity" with "kinase activity" eliminating the basis of the rejection. However, applicant has not addressed the rejection directed to "any substrate". Mere amendment of claims to recite "kinase activity" does not overcome the non-enablement issues raised in the previous and the present rejections. Therefore, Examiner continues to maintain the above rejection.

Claims 1-7, 11-20, 24-29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-7, 11-20, 24-29 are directed to a method of screening a candidate compound for its ability to inhibit or agonize the (kinase) activity of the polypeptides SEQ ID NO:5, 14, 11, 13, 6, 15 etc. Claims 1-7, 11-20, 24-29 are rejected under this section of 35 USC 112 because the claims are directed to the use of a genus of polypeptides whose specific function has not been disclosed in the specification. No information, has been provided by applicants which would indicate that they had possession of the claimed genus of polypeptides for use in the above method. The specification does not contain any disclosure of the specific function (i.e., the specific substrates that are phosphorylated by the polypeptides) of the polypeptide sequences within the scope of the claimed genus. The genus of polypeptides claimed for use in the above methods is a variable genus which can have a wide variety of phosphorylating functions (i.e., encompasses the phosphorylation of a wide variety of substrates). Therefore many functionally unrelated polypeptides are encompassed within the scope of these claims (i.e., those which have a varied phosphorylation activity). The function allocated to the polypeptides is not representative of the entire genus. The specification does not disclose even a single specific function (a specific kinase reaction) of the genus of the polypeptides used in the above claimed method which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot

reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

As discussed in the written description guidelines the written description requirement for the use of a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe sufficient variety to reflect the variation within the genus. The identifying characteristic of the polypeptides used in the claimed method, i.e., kinase activity, does not include sufficient characteristics to limit the claimed genus to proteins which are not highly variable in function. The claims include species which vary widely in their kinase function. Therefore, the species within the genus are highly variable in function and are not representative. While above claims add a single characteristic to the limitations of the genus of each of these claims (i.e., kinase activity), this characteristic, by itself is sufficient to change the fact that the claims include proteins which are highly variable in that function. Thus for all the reasons discussed, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

In response to the previous rejection of claims 8-9, 13, 21-22, 26 and 30 as not described, applicant has cancelled claims 8-9, 21-22 and 30 and amended claims 13 and 26 which does overcome the previous rejection. However, applicant's amendment of above claims by introduction of the phrase "kinase activity", raises new written description issues. Hence the above rejection.

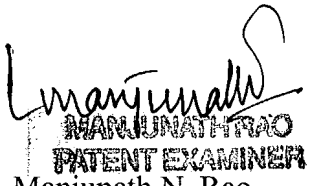
Conclusion

None of the claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 703-306-5681. The examiner can normally be reached on 7.30 a.m. to 4.00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-306-0196.



Manjunath N. Rao
February 20, 2004